

SEQUENCE LISTING

<110> KYOWA HAKKO KOGYO CO., LTD

<120> AGENT FOR TREATING ARTHRITIS

<130> 1442

<150> JP2001-400677

<151> 2001-12-28

<160> 51

<170> PatentIn version 3.1

<210> 1

<211> 420

<212> DNA

<213> Mus musculus

<220>

<221> source

<222> (1)..(420)

<223> /organism="Mus musculus"

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<221> CDS

<222> (1)..(420)

<220>

<221> sig_peptide

<222> (1)..(57)

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Met Glu Trp Ile Trp Ile Phe Leu Phe Phe Leu Ser Gly Thr Thr Gly	
1 5 10 15	

gtc tac tcc cag gtt cag ctg cag cag tct gga gct gag gtg gcg agg	96
Val Tyr Ser Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Val Ala Arg	
20 25 30	

ccc ggg gct tca gtg aaa ctg tcc tgc aag gct tct ggc tac acc ttc	144
Pro Gly Ala Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Thr Phe	
35 40 45	

act gac tac tat cta aac tgg gtg aag cag agg tct gga cag ggc ctt	192
Thr Asp Tyr Tyr Leu Asn Trp Val Lys Gln Arg Ser Gly Gln Gly Leu	
50 55 60	

gag tgg att gga gag att gat cct gga agt gat agt ata tat tat aat	240
Glu Trp Ile Gly Glu Ile Asp Pro Gly Ser Asp Ser Ile Tyr Tyr Asn	
65 70 75 80	

gaa aac ttg gag ggc agg gcc aca ctg act gca gac aaa tcc tcc agc	288
Glu Asn Leu Glu Gly Arg Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser	
85 90 95	

aca gcc tac atg cag ctc aac agc ctg aca tct gag gac tct gca gtc	336
Thr Ala Tyr Met Gln Leu Asn Ser Leu Thr Ser Glu Asp Ser Ala Val	
100 105 110	

tat ttc tgt gca aga tat ggg tat tct aga tac gac gta agg ttt gtc	384
Tyr Phe Cys Ala Arg Tyr Gly Tyr Ser Arg Tyr Asp Val Arg Phe Val	
115 120 125	

tac tgg ggc caa ggg act ctg gtc act gtc tct aca	420
Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Thr	
130 135 140	

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 <212> PRT
 <213> Mus musculus

<220>
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 <222> (1)..(19)

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1 5 10 15	

Val Tyr Ser Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Val Ala Arg	
20 25 30	

Pro Gly Ala Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Thr Phe	
35 40 45	

Thr Asp Tyr Tyr Leu Asn Trp Val Lys Gln Arg Ser Gly Gln Gly Leu	
50 55 60	

Glu Trp Ile Gly Glu Ile Asp Pro Gly Ser Asp Ser Ile Tyr Tyr Asn	
65 70 75 80	

Glu Asn Leu Glu Gly Arg Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser	
85 90 95	

Thr Ala Tyr Met Gln Leu Asn Ser Leu Thr Ser Glu Asp Ser Ala Val	
100 105 110	

Tyr Phe Cys Ala Arg Tyr Gly Tyr Ser Arg Tyr Asp Val Arg Phe Val	
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130		135		140
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Met Lys Leu Pro Val Arg Leu Leu Val Leu Met Phe Trp Ile Pro Ala				
1 5 10 15				
tcc agg agt gat gtt ttg atg acc caa act cca ctc tcc ctg cct gtc				96
Ser Arg Ser Asp Val Leu Met Thr Gln Thr Pro Leu Ser Leu Pro Val				
20 25 30				
agt ctt gga gat caa gcc tcc atc tct tgc aga tct agt cag agt ctt				144
Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu				
35 40 45				
gta cat agt aat gga aga acc tat tta gaa tgg tac ctg cag aaa cct				192
Val His Ser Asn Gly Arg Thr Tyr Leu Glu Trp Tyr Leu Gln Lys Pro				
50 55 60				
ggc cag tca cca aag gtc ctg atc tac aaa gtt tcc aac cga att tct				240
Gly Gln Ser Pro Lys Val Leu Ile Tyr Lys Val Ser Asn Arg Ile Ser				
65 70 75 80				
ggg gtc cca gac agg ttc agt ggc agt gga tca ggg aca gat ttc aca				288
Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr				
85 90 95				
ctc aaa atc agc aga gtg gag gct gag gat ctg gga gtt tat ttc tgc				336
Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Phe Cys				
100 105 110				
ttt cag ggt tca cat gtt ccg tac acg ttc gga ggg ggg acc aag ctg				384
Phe Gln Gly Ser His Val Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu				

115
gaa ata aaa
Glu Ile Lys
130

120

125

393

<210> 4
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<220>
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<222> (1)..(19)

<400> 4
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1 5 10 15
Ser Arg Ser Asp Val Leu Met Thr Gln Thr Pro Leu Ser Leu Pro Val
20 25 30
Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu
35 40 45
Val His Ser Asn Gly Arg Thr Tyr Leu Glu Trp Tyr Leu Gln Lys Pro
50 55 60
Gly Gln Ser Pro Lys Val Leu Ile Tyr Lys Val Ser Asn Arg Ile Ser
65 70 75 80
Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
85 90 95
Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Phe Cys
100 105 110
Phe Gln Gly Ser His Val Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu
115 120 125
Glu Ile Lys
130

<210> 5
<211> 121
<212> PRT
<213> Mus musculus

<400> 5
Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Val Ala Arg Pro Gly Ala
1 5 10 15
Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
20 25 30

Tyr Leu Asn Trp Val Lys Gln Arg Ser Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Glu Ile Asp Pro Gly Ser Asp Ser Ile Tyr Tyr Asn Glu Asn Leu
50 55 60

Glu Gly Arg Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr
65 70 75 80

Met Gln Leu Asn Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys
85 90 95

Ala Arg Tyr Gly Tyr Ser Arg Tyr Asp Val Arg Phe Val Tyr Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Thr
115 120

<210> 6
<211> 112
<212> PRT
<213> Mus musculus

<400> 6
Asp Val Leu Met Thr Gln Thr Pro Leu Ser Leu Pro Val Ser Leu Gly
1 5 10 15

Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Gly Arg Thr Tyr Leu Glu Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Lys Val Leu Ile Tyr Lys Val Ser Asn Arg Ile Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Phe Cys Phe Gln Gly
85 90 95

Ser His Val Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys

100

105

110

<210> 7
<211> 5
<212> PRT
<213> Mus musculus

<400> 7
Asp Tyr Tyr Leu Asn
1 5

<210> 8
<211> 17
<212> PRT
<213> Mus musculus

<400> 8
Glu Ile Asp Pro Gly Ser Asp Ser Ile Tyr Tyr Asn Glu Asn Leu Glu
1 5 10 15

Gly

<210> 9
<211> 12
<212> PRT
<213> Mus musculus

<400> 9
Tyr Gly Tyr Ser Arg Tyr Asp Val Arg Phe Val Tyr
1 5 10

<210> 10
<211> 16
<212> PRT
<213> Mus musculus

<400> 10
Arg Ser Ser Gln Ser Leu Val His Ser Asn Gly Arg Thr Tyr Leu Glu
1 5 10 15

<210> 11
<211> 7
<212> PRT
<213> Mus musculus

<400> 11
Lys Val Ser Asn Arg Ile Ser
1 5

<210> 12

<211> 9
<212> PRT
<213> Mus musculus

<400> 12
Phe Gln Gly Ser His Val Pro Tyr Thr
1 5

<210> 13
<211> 22
<212> DNA
<213> Artificial Sequence

<220>
<223> a primer for amplification of KM1334 VH

<400> 13
ctgaattcgc ggccgctagt cc 22

<210> 14
<211> 39
<212> DNA
<213> Artificial Sequence

<220>
<223> a primer for amplification of KM1334 VH

<400> 14
atgggccctt ggtggaggct gtagagacag tgaccagag 39

<210> 15
<211> 22
<212> DNA
<213> Artificial Sequence

<220>
<223> a primer for amplification of KM1334 VL

<400> 15
ctgaattcgc ggccgctgct gt 22

<210> 16
<211> 28
<212> DNA
<213> Artificial Sequence

<220>
<223> a primer for amplification of KM1334 VL

<400> 16
atcgtacgtt ttatttccag cttggtcc 28

<210> 17
<211> 25
<212> PRT
<213> Artificial Sequence

<220>
<223> human FGF-8 peptide (amino acids residues 23-46) added an
cysteine residue at its C-terminus

<400> 17
Gln Val Thr Val Gln Ser Ser Pro Asn Phe Thr Gln His Val Arg Glu
1 5 10 15

Gln Ser Leu Val Thr Asp Gln Leu Cys
20 25

<210> 18
<211> 121
<212> PRT
<213> Artificial Sequence

<220>
<223> HV.0, a designed amino acid sequence of VH of
an anti-FGF-8 CDR-grafted neutralizing antibody

<400> 18
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
20 25 30

Tyr Leu Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Glu Ile Asp Pro Gly Ser Asp Ser Ile Tyr Tyr Asn Glu Asn Leu
50 55 60

Glu Gly Arg Val Thr Ile Thr Ala Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Gly Tyr Ser Arg Tyr Asp Val Arg Phe Val Tyr Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 19
<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<223> LV.0, a designed amino acid sequence of VL of
an anti-FGF-8 CDR-grafted neutralizing antibody

<400> 19
Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
1 5 10 15

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Gly Arg Thr Tyr Leu Glu Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Gln Leu Leu Ile Tyr Lys Val Ser Asn Arg Ile Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Phe Gln Gly
85 90 95

Ser His Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105 110

<210> 20
<211> 121
<212> PRT
<213> Artificial Sequence

<220>
<223> HV.6, a designed amino acid sequence of VH of
an anti-FGF-8 CDR-grafted neutralizing antibody

<400> 20
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Ala Arg Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
20 25 30

Tyr Leu Asn Trp Val Arg Gln Arg Ser Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Glu Ile Asp Pro Gly Ser Asp Ser Ile Tyr Tyr Asn Glu Asn Leu
50 55 60

Glu Gly Arg Val Thr Ile Thr Ala Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Phe Cys
85 90 95

Ala Arg Tyr Gly Tyr Ser Arg Tyr Asp Val Arg Phe Val Tyr Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 21
<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<223> LV.6, a designed amino acid sequence of VL of
an anti-FGF-8 CDR-grafted neutralizing antibody

<400> 21
Asp Val Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Ser Leu Gly
1 5 10 15

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Gly Arg Thr Tyr Leu Glu Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Lys Val Leu Ile Tyr Lys Val Ser Asn Arg Ile Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Phe Cys Phe Gln Gly
85 90 95

Ser	His	Val	Pro	Tyr	Thr	Phe	Gly	Gln	Gly	Thr	Lys	Val	Glu	Ile	Lys
		100						105					110		

<210> 22
 <211> 504
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> a DNA encoding HV.0

<220>
 <221> CDS
 <222> (47)..(466)

<220>
 <221> sig_peptide
 <222> (47)..(103)

<400> 22
 caggaaacag ctatgacgaa ttcgcggccg cacactgact ctaacc atg gaa tgg 55
 Met Glu Trp

atc tgg atc ttt ctc ttc ttc ctc tca gga act aca ggt gtc tac tcc 103
 Ile Trp Ile Phe Leu Phe Phe Leu Ser Gly Thr Thr Gly Val Tyr Ser
 -15 -10 -5 -1

cag gtg cag ctg gtg cag tct ggg gct gag gtg aag aag ccc ggg gcc 151
 Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15

tca gtg aag gtc tcc tgc aag gct tct gga tac acc ttc act gac tac 199
 Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
 20 25 30

tat cta aac tgg gtg cgg cag gcc ccc gga caa ggg ctt gag tgg atg 247
 Tyr Leu Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
 35 40 45

gga gag atc gat cct gga agt gat agt ata tat tat aat gaa aac ttg 295
 Gly Glu Ile Asp Pro Gly Ser Asp Ser Ile Tyr Tyr Asn Glu Asn Leu
 50 55 60

gag ggc aga gtc acg att acc gcg gac aca tcc acg agc aca gcc tac 343
 Glu Gly Arg Val Thr Ile Thr Ala Asp Thr Ser Thr Ser Thr Ala Tyr
 65 70 75 80

atg gag ctg agc agc ctg aga tct gag gac acg gcc gtg tat tac tgt 391
 Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

gcg aga tat ggg tat tct aga tac gac gta agg ttt gtc tac tgg ggc 439
 Ala Arg Tyr Gly Tyr Ser Arg Tyr Asp Val Arg Phe Val Tyr Trp Gly

100	105	110	
cag gga acc ctg gtc acc gtc tcc tca gcctccacca agggcccact			486
Gln Gly Thr Leu Val Thr Val Ser Ser			
115	120		
agtcgtgact gggaaaac			504
<210>	23		
<211>	141		
<212>	DNA		
<213>	Artificial Sequence		
<220>			
<223>	a synthetic DNA for construction of a DNA encoding HV.0		
<400>	23		
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gatctttctc ttcttctct caggaactac aggtgtctac tcccaggtgc agctggtgca			120
gtctggggct gaggtgaaga a			141
<210>	24		
<211>	141		
<212>	DNA		
<213>	Artificial Sequence		
<220>			
<223>	a synthetic DNA for construction of a DNA encoding HV.0		
<400>	24		
aggatcgatc tctcccatcc actcaagccc ttgtccgggg gcctgccgca cccagtttag			60
atagtagtca gtgaaggtgt atccagaagc cttgcaggag accttcactg aggccccggg			120
cttcttcacc tcagccccag a			141
<210>	25		
<211>	141		
<212>	DNA		
<213>	Artificial Sequence		
<220>			
<223>	a synthetic DNA for construction of a DNA encoding HV.0		
<400>	25		
ggatgggaga gatcgatcct ggaagtgata gtatatatta taatgaaaac ttggagggca			60
gagtcacgat taccgcggac acatccacga gcacagccta catggagctg agcagcctga			120
gatctgagga cacggccgtg t			141

<210> 26
 <211> 141
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> a synthetic DNA for construction of a DNA encoding HV.0

<400> 26
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 ccctggcccc agtagacaaa cttacgtcg tatctagaat acccatatct cgcacagtaa 120
 tacacggccg tgcctcaga t 141

<210> 27
 <211> 504
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> a DNA encoding HV.6

<220>
 <221> CDS
 <222> (47)..(466)

<220>
 <221> sig_peptide
 <222> (47)..(103)

<400> 27
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 Met Glu Trp

atc tgg atc ttt ctc ttc ttc ctc tca gga act aca ggt gtc tac tcc 103
 Ile Trp Ile Phe Leu Phe Phe Leu Ser Gly Thr Thr Gly Val Tyr Ser
 -15 -10 -5 -1

cag gtg cag ctg gtg cag tct ggg gct gag gtg gcg agg ccc ggg gcc 151
 Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Ala Arg Pro Gly Ala
 1 5 10 15

tca gtg aag gtc tcc tgc aag gct tct gga tac acc ttc act gac tac 199
 Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
 20 25 30

tat cta aac tgg gtg cgg cag agg tct gga caa ggg ctt gag tgg att 247
 Tyr Leu Asn Trp Val Arg Gln Arg Ser Gly Gln Gly Leu Glu Trp Ile
 35 40 45

gga gag atc gat cct gga agt gat agt ata tat tat aat gaa aac ttg 295
 Gly Glu Ile Asp Pro Gly Ser Asp Ser Ile Tyr Tyr Asn Glu Asn Leu
 50 55 60

gag ggc aga gtc acg att acc gcg gac aca tcc acg agc aca gcc tac	343
Glu Gly Arg Val Thr Ile Thr Ala Asp Thr Ser Thr Ser Thr Ala Tyr	
65 70 75 80	

atg gag ctg agc agc ctg aga tct gag gac acg gcc gtg tat ttc tgt	391
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Phe Cys	
85 90 95	

gcg aga tat ggg tat tct aga tac gac gta agg ttt gtc tac tgg ggc	439
Ala Arg Tyr Gly Tyr Ser Arg Tyr Asp Val Arg Phe Val Tyr Trp Gly	
100 105 110	

cag gga acc ctg gtc acc gtc tcc tca gcctccacca agggcccact	486
Gln Gly Thr Leu Val Thr Val Ser Ser	
115 120	

agtcgtgact gggaaaac	504
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<210> 28
 <211> 141
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> a synthetic DNA for construction of a DNA encoding HV.6

<400> 28	
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gatctttctc ttcttcctct caggaactac aggtgtctac tcccaggtgc agctggtgca	120
gtctggggct gaggtggcga g	141

<210> 29
 <211> 141
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> a synthetic DNA for construction of a DNA encoding HV.6

<400> 29	
aggatcgatc tctccaatcc actcaagccc ttgtccagac ctctgccgca cccagtttag	60
atagtagtca gtgaaggtgt atccagaagc cttgcaggag accttcactg aggccccggg	120
cctcgccacc tcagccccag a	141

<210> 30
 <211> 141
 <212> DNA
 <213> Artificial Sequence

<220>

<223> a synthetic DNA for construction of a DNA encoding HV.6

<400> 30

ggattggaga gatcgatcct ggaagtgata gtatatatta taatgaaaac ttggagggca 60

gagtcacgat taccgcggaac acatccacga gcacagccta catggagctg agcagcctga 120

gatctgagga cacggccgtg t 141

<210> 31

<211> 141

<212> DNA

<213> Artificial Sequence

<220>

<223> a synthetic DNA for construction of a DNA encoding HV.6

<400> 31

gttttcccag tcacgactag tggggcccttg gtggaggctg aggagacggt gaccaggggt 60

ccctggcccc agtagacaaa cttacgtcg tatctagaat acccatatct cgcacagaaa 120

tacacggccg tgtcctcaga t 141

<210> 32

<211> 459

<212> DNA

<213> Artificial Sequence

<220>

<223> a DNA encoding LV.0

<220>

<221> CDS

<222> (40)..(432)

<220>

<221> sig_peptide

<222> (40)..(96)

<400> 32

caggaaacag ctatgacgaa ttcaggttgc ctctcaaa atg aag ttg cct gtt 54
Met Lys Leu Pro Val
-15

agg ctg ttg gtg ctg atg ttc tgg att cct gct tcc agg agt gat atc 102
Arg Leu Leu Val Leu Met Phe Trp Ile Pro Ala Ser Arg Ser Asp Ile
-10 -5 -1 1

gtg atg act cag tct cca ctc tcc ctg ccc gtc acc cct gga gag ccg 150
Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly Glu Pro
5 10 15

gcc tcc atc tcc tgc aga tct agt cag agt ctt gta cat agt aat gga	198
Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser Asn Gly	
20 25 30	

aga acc tat tta gaa tgg tac ctg cag aag cca ggc cag tct cca cag	246
Arg Thr Tyr Leu Glu Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro Gln	
35 40 45 50	

ctc ctg atc tat aaa gtt tcc aac cga att tct ggg gtc cca gac agg	294
Leu Leu Ile Tyr Lys Val Ser Asn Arg Ile Ser Gly Val Pro Asp Arg	
55 60 65	

ttc agt ggc agt gga tcc ggg aca gat ttc aca ctg aaa atc agc agg	342
Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg	
70 75 80	

gtg gag gct gag gac gtc ggg gtt tat tac tgc ttt cag ggt tca cat	390
Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Phe Gln Gly Ser His	
85 90 95	

gtt ccg tac acg ttc ggc caa ggg acc aag gtg gaa atc aaa	432
Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys	
100 105 110	

cgtagcacta gtcgtgactg ggaaaac	459
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<210> 33
 <211> 130
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> a synthetic DNA for construction of a DNA encoding LV.0

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caggaaacag ctatgacgaa ttcaggttgc ctctcaaaa tgaagttgcc tgtaggctg	60

ttggtgctga tgttctggat tcctgcttcc aggagtata tcgtgatgac tcagtctcca	120
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ctctccctgc	130
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<210> 34
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 <212> DNA
 <213> Artificial Sequence

<220>
 <223> a synthetic DNA for construction of a DNA encoding LV.0

<400> 34	
agactggcct ggcttctgca ggtaccattc taaataggtt cttccattac tatgtacaag	60

actctgacta gatctgcagg agatggaggc cggctctcca ggggtgacgg gcagggagag	120
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tggagactga	130
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<210> 35
<211> 130
<212> DNA
<213> Artificial Sequence

<220>
<223> a synthetic DNA for construction of a DNA encoding LV.0

<400> 35
tgcagaagcc aggccagtct ccacagctcc tgatctataa agtttccaac cgaatttctg 60
gggtcccaga caggttcagt ggcagtggat cggggacaga tttcacactg aaaatcagca 120
gggtggaggc 130

<210> 36
<211> 129
<212> DNA
<213> Artificial Sequence)

<220>
<223> a synthetic DNA for construction of a DNA encoding LV.0

<400> 36
gttttccag tcacgactag tcgtacgttt gatttccacc ttggtccctt ggccgaacgt 60
gtacggaaca tgtgaaccct gaaagcagta ataaaccccg acgtcctcag cctccaccct 120
gctgatttt 129

<210> 37
<211> 459
<212> DNA
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<220>
<223> a DNA encoding LV.6

<220>
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<222> (40)..(432)

<220>
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<222> (40)..(96)

<400> 37
caggaaacag ctatgacgaa ttcaggttgc ctctcaaa atg aag ttg cct gtt 54
Met Lys Leu Pro Val
-15

agg ctg ttg gtg ctg atg ttc tgg att cct gct tcc agg agt gat gtt 102
Arg Leu Leu Val Leu Met Phe Trp Ile Pro Ala Ser Arg Ser Asp Val

	-10		-5		-1	1	
gtg atg act cag tct cca ctc tcc ctg ccc gtc agt ctt gga gag ccg							150
Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Ser Leu Gly Glu Pro							
	5		10		15		
gcc tcc atc tcc tgc aga tct agt cag agt ctt gta cat agt aat gga							198
Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser Asn Gly							
	20		25		30		
aga acc tat tta gaa tgg tac ctg cag aag cca ggc cag tct cca aag							246
Arg Thr Tyr Leu Glu Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro Lys							
	35		40		45		50
gtc ctg atc tat aaa gtt tcc aac cga att tct ggg gtc cca gac agg							294
Val Leu Ile Tyr Lys Val Ser Asn Arg Ile Ser Gly Val Pro Asp Arg							
		55		60		65	
ttc agt ggc agt gga tcc ggg aca gat ttc aca ctg aaa atc agc agg							342
Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg							
	70		75		80		
gtg gag gct gag gac gtc ggg gtt tat ttc tgc ttt cag ggt tca cat							390
Val Glu Ala Glu Asp Val Gly Val Tyr Phe Cys Phe Gln Gly Ser His							
	85		90		95		
gtt ccg tac acg ttc ggc caa ggg acc aag gtg gaa atc aaa							432
Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys							
	100		105		110		
cgtagcacta gtcgtgactg ggaaaac							459

<210> 38
 <211> 130
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> a synthetic DNA for construction of a DNA encoding LV.6

<400> 38	
caggaaacag ctatgacgaa ttcaggttgc ctctcaaaa tgaagttgcc tgtaggctg	60
ttggtgctga tgttctggat tctgtctcc aggagtgatg ttgtgatgac tcagtctcca	120
ctctccctgc	130

<210> 39
 <211> 130
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> a synthetic DNA for construction of a DNA encoding LV.6

<400> 39
agactggcct ggcttctgca ggtaccattc taaatagggtt cttccattac tatgtacaag 60
actctgacta gatctgcagg agatggaggc cggctctcca agactgacgg gcagggagag 120
tggagactga 130

<210> 40
<211> 130
<212> DNA
<213> Artificial Sequence

<220>
<223> a synthetic DNA for construction of a DNA encoding LV.6

<400> 40
tgcagaagcc aggccagtct ccaaagggtcc tgatctataa agtttccaac cgaatttctg 60
gggtcccaga caggttcagt ggcagtggat ccgggacaga tttcacactg aaaatcagca 120
gggtggaggc 130

<210> 41
<211> 129
<212> DNA
<213> Artificial Sequence

<220>
<223> a synthetic DNA for construction of a DNA encoding LV.6

<400> 41
gttttcccag tcacgactag tcgtacgttt gatttccacc ttggtccctt ggccgaacgt 60
gtacggaaca tgtgaaccct gaaagcagaa ataaaccccg acgtcctcag cctccaccct 120
gctgatttt 129

<210> 42
<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<223> LV.4-1, a designed amino acid sequence of VL of
an anti-FGF-8 CDR-grafted neutralizing antibody

<400> 42
Asp Val Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
1 5 10 15

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser

20

25

30

Asn Gly Arg Thr Tyr Leu Glu Trp Tyr Leu Gln Lys Pro Gly Gln Ser
 35 40 45

Pro Lys Val Leu Ile Tyr Lys Val Ser Asn Arg Ile Ser Gly Val Pro
 50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
 65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Phe Cys Phe Gln Gly
 85 90 95

Ser His Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
 100 105 110

<210> 43

<211> 112

<212> PRT

<213> Artificial Sequence

<220>

<223> LV.4-2, a designed amino acid sequence of VL of
 an anti-FGF-8 CDR-grafted neutralizing antibody

<400> 43

Asp Val Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Ser Leu Gly
 1 5 10 15

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
 20 25 30

Asn Gly Arg Thr Tyr Leu Glu Trp Tyr Leu Gln Lys Pro Gly Gln Ser
 35 40 45

Pro Gln Leu Leu Ile Tyr Lys Val Ser Asn Arg Ile Ser Gly Val Pro
 50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
 65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Phe Cys Phe Gln Gly
 85 90 95

Ser His Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105 110

<210> 44
<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<223> LV.3-1, a designed amino acid sequence of VL of
an anti-FGF-8 CDR-grafted neutralizing antibody

<400> 44
Asp Val Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
1 5 10 15

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Gly Arg Thr Tyr Leu Glu Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Gln Val Leu Ile Tyr Lys Val Ser Asn Arg Ile Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Phe Cys Phe Gln Gly
85 90 95

Ser His Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105 110

<210> 45
<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<223> LV.3-2, a designed amino acid sequence of VL of
an anti-FGF-8 CDR-grafted neutralizing antibody

<400> 45
Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Ser Leu Gly
1 5 10 15

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser

20

25

30

Asn Gly Arg Thr Tyr Leu Glu Trp Tyr Leu Gln Lys Pro Gly Gln Ser
 35 40 45

Pro Gln Leu Leu Ile Tyr Lys Val Ser Asn Arg Ile Ser Gly Val Pro
 50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
 65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Phe Cys Phe Gln Gly
 85 90 95

Ser His Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
 100 105 110

<210> 46

<211> 112

<212> PRT

<213> Artificial Sequence

<220>

<223> LV.2-1, a designed amino acid sequence of VL of
 an anti-FGF-8 CDR-grafted neutralizing antibody

<400> 46

Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
 1 5 10 15

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
 20 25 30

Asn Gly Arg Thr Tyr Leu Glu Trp Tyr Leu Gln Lys Pro Gly Gln Ser
 35 40 45

Pro Gln Val Leu Ile Tyr Lys Val Ser Asn Arg Ile Ser Gly Val Pro
 50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
 65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Phe Cys Phe Gln Gly
 85 90 95

Ser His Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105 110

<210> 47
<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<223> LV.2-2, a designed amino acid sequence of VL of
an anti-FGF-8 CDR-grafted neutralizing antibody

<400> 47
Asp Val Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
1 5 10 15

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Gly Arg Thr Tyr Leu Glu Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Gln Leu Leu Ile Tyr Lys Val Ser Asn Arg Ile Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Phe Cys Phe Gln Gly
85 90 95

Ser His Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105 110

<210> 48
<211> 39
<212> DNA
<213> Artificial Sequence

<220>
<223> a primer for construction of DNA encoding LV.3-1

<400> 48
atggtacctg cagaagccag gccagtctcc acaggtcct

<210> 49

<211> 39
<212> DNA
<213> Artificial Sequence

<220>
<223> a primer for construction of DNA encoding LV.2-2

<400> 49
atggtacctg cagaagccag gccagtctcc acagctcct

39

<210> 50
<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<223> LV.4-3, a designed amino acid sequence of VL of
an anti-FGF-8 CDR-grafted neutralizing antibody

<400> 50
Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Ser Leu Gly
1 5 10 15

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Gly Arg Thr Tyr Leu Glu Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Gln Val Leu Ile Tyr Lys Val Ser Asn Arg Ile Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Phe Cys Phe Gln Gly
85 90 95

Ser His Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105 110

<210> 51
<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<223> LV.3-3, a designed amino acid sequence of VL of
an anti-FGF-8 CDR-grafted neutralizing antibody

<400> 51

Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Ser Leu Gly
1 5 10 15

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Gly Arg Thr Tyr Leu Glu Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Gln Val Leu Ile Tyr Lys Val Ser Asn Arg Ile Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Phe Gln Gly
85 90 95

Ser His Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105 110